

ADC Oncology 2026: Risks, Catalysts & Scenario Analysis

May 14, 2026

Operator Intelligence™

Merck/Daiichi Sankyo Collaboration · DXd Platform · Emerging Competitors · BD/M&A Implications

EXECUTIVE SNAPSHOT

- The Merck/Daiichi Sankyo DXd platform is the single most consequential ADC pipeline in oncology; its October 2026 I-DXd PDUFA in SCLC is the year's defining binary regulatory event.
- Keytruda combination strategy is both the bull case multiplier and the platform's largest unproven variable — payer and regulatory reception of combo labeling will shape peak-sales forecasts across 4+ assets.
- Manufacturing capacity changes announced May 2026 introduce a near-term supply-risk overhang that prior ADC launches (Enhertu 2019–2021) have shown can materially constrain uptake curves in the first 12–18 months.
- Chinese ADC entrants (Kelun-Biotech, RemeGen) are compressing the global differentiation window faster than most Western BD models assume; ex-US licensing economics are repricing in real time.
- **Core recommendation:** Acquirers and partners should price the DXd platform at base-case approval probabilities but stress-test for supply-limited launches; the asymmetric risk/reward sits in HER3-DXd and CDH6, not in assets already approaching peak valuation.

1. Strategic Context: Why the DXd Platform Is a Singular Event

The Merck–Daiichi Sankyo collaboration, consummated in a deal structure that committed up to \$22 billion across milestone payments for co-development rights to three DXd assets (I-DXd, R-DXd, and HER3-DXd), represents the largest single ADC platform bet in pharmaceutical history. The strategic logic was unambiguous: Merck needed a post-Keytruda revenue bridge as IgG-PD-1 monotherapy saturates across indications; Daiichi needed capital and commercial infrastructure to prosecute a multi-tumor strategy that its own balance sheet could not sustain at the required trial velocity. The result is a partnership where the clinical and regulatory timelines of multiple independent assets now run in parallel, creating both upside optionality and a concentration of execution risk that most large-cap pharma portfolios do not carry.

The broader ADC market context amplifies this. The FDA has demonstrated consistent willingness to use Accelerated Approval pathways for ADCs with single-arm trial data in heavily pre-treated populations, as established through the

approval precedents of Enhertu in HER2-low breast cancer and sacituzumab govitecan in TNBC. The CMS coverage framework — through National Coverage Determinations and MAC-level Local Coverage Determinations — has generally followed FDA labeling for these agents with limited restriction, although the introduction of the Inflation Reduction Act drug negotiation program is beginning to create payer-side pressure on ADCs entering large indications. This macro environment means the DXd platform's regulatory path is well-trodden, but its commercial path is increasingly contested.

Enhertu (trastuzumab deruxtecan) and Datroway (datopotamab deruxtecan), developed under the earlier AstraZeneca–Daiichi Sankyo collaboration, serve as the calibration benchmarks for every projection in this analysis. Enhertu's trajectory — from accelerated approval to broad HER2-positive and HER2-low labeling with OS data — defines what a DXd asset at peak execution looks like. Datroway's slower uptake in TROP2-positive NSCLC against entrenched Keytruda combinations illustrates the floor. The Merck collaboration assets sit on a spectrum between these two poles depending on indication-specific unmet need and the strength of the combination hypothesis.

Operator Precedent — Enhertu Launch Calibration: Enhertu's 2019 accelerated approval in HER2+ gastric cancer was followed by 18 months of constrained supply due to lyophilization capacity limitations at Daiichi's Odawara facility. Peak quarterly revenues did not normalize until AZ's contribution to contract manufacturing was fully operational. The I-DXd SCLC launch, if approved October 2026, faces an analogous risk profile given the May 2026 manufacturing plan updates — operators should model a 12-month ramp delay as the base case, not the exception.

So what / Decision implied: Anyone building a commercial model on DXd approvals in 2026–2027 must separate the approval probability from the revenue ramp assumption. These are independent variables, and conflating them was the single largest error in early Enhertu commercial forecasts.

2. Key Milestones & Catalyst Timeline (2026–2028)

The table below maps each DXd and competitive ADC asset to its most consequential clinical and regulatory catalysts through 2028. The timeline is dense — nine potential binary regulatory or data events across 36 months — and the sequencing matters as much as the individual outcomes, because early approvals create label-expansion momentum and early failures create cross-asset skepticism in oncology committees.

Asset / Program	Target	Indication	Catalyst	Timing	Approval Probability (Katogen Est.)
Ifinatamab deruxtecan (I-DXd)	B7-H3	SCLC (3L+)	FDA PDUFA / Accelerated Approval decision	October 2026	70–75%
I-DXd	B7-H3	SCLC (combo Keytruda, 1L)	Phase 3 IDEate-Lung03 interim data	H2 2027	Confirmatory (approval-gating)
Patritumab deruxtecan (HER3-DXd)	HER3	NSCLC (EGFR-mut, post-osimertinib)	NDA submission / Priority Review decision	H1 2027	65–70%
HER3-DXd	HER3	Breast cancer (HR+/HER2-)	Phase 3 enrollment completion; data H2 2027	2027–2028	Too early to estimate
Raludotatug deruxtecan (R-DXd)	CDH6	Ovarian cancer (platinum-resistant)	Phase 2/3 interim OS data	H1 2027	Speculative; CDH6 biology unproven at scale

Sacituzumab tirumotecan (Sac-TMT)	TROP2	HR+/HER2- breast cancer	Phase 3 OptiTROP-Breast01 data; NDA 2026–2027	2026 data; 2027 PDUFA est.	60–65% (crowded field risk)
Enhertu (T-DXd) — AZ/DSC benchmark	HER2	HER2-low/ultralow breast; NSCLC; gastric	Label expansions (DESTINY-Breast09, -Lung04)	2026–2027 rolling	High (confirmatory studies, not first-in-class)
Datroway (Dato-DXd) — AZ/DSC benchmark	TROP2	NSCLC; HR+ breast	TROPION-Breast01 OS maturity; NSCLC label defense	2026–2027	Moderate; OS data is the pivotal variable
Kelun-Biotech / MSD (SKB264)	TROP2	NSCLC; TNBC	US Phase 3 data readout (licensed to MSD)	2027	Uncertain; linker-payload differentiation unclear
RemeGen (RC48 disitamab vedotin)	HER2	Urothelial; gastric	US NDA / FDA review	2026–2027	55–60%; tolerability data is the gating issue

The concentration of pivotal data in H1 2027 is not coincidental — it reflects a 2023–2024 trial enrollment surge across the industry that is now maturing. For operators and BD teams, this creates a 9–12 month window starting Q4 2026 where the risk-adjusted valuation of ADC platforms will be re-rated by the market in rapid succession. Missing a single major readout in this window — particularly the I-DXd PDUFA or HER3-DXd NDA — resets the Merck collaboration's near-term narrative despite the long-term pipeline quality.

So what / Decision implied: BD teams should treat Q4 2026 through Q2 2027 as a concentrated due-diligence window, not a monitoring period. Assets with 2028+ data timelines can be evaluated on fundamentals; assets with 2026–2027 binary events require scenario-weighted valuation models, not DCF averages.

3. Milestone Risk Matrix

The following risk matrix scores each major catalyst on two dimensions: regulatory/clinical probability of a positive outcome (x-axis equivalent) and strategic impact on the broader DXd platform franchise (y-axis equivalent). High-impact, moderate-probability events define where management and investor attention should concentrate; low-impact events, regardless of probability, are execution items rather than strategic pivots.

Catalyst Event	Probability of Positive Outcome	Strategic Impact on Platform (1–5)	Risk Type	Primary Risk Driver
I-DXd SCLC FDA approval (Oct 2026)	High (70–75%)	★★★★★ (5)	Binary regulatory	Single-arm data sufficiency; ILD signal in label
HER3-DXd NDA acceptance + approval (2027)	Moderate-High (65–70%)	★★★★★ (5)	Binary regulatory + competitive	Osimertinib combo sequencing; EGFR-mut market crowding
I-DXd + Keytruda 1L SCLC Phase 3 interim	Moderate (50–60%)	★★★★★ (5)	Clinical + commercial	Combo incremental OS benefit over atezolizumab+chemo

R-DXd CDH6 ovarian Phase 2/3 interim	Low-Moderate (35–45%)	★★★★ (4)	Clinical / novel target	CDH6 target expression heterogeneity; prior ADC failures in ovarian
Sac-TMT TROP2 HR+ breast NDA (2027)	Moderate (60–65%)	★★★ (3)	Competitive / differentiation	Datroway and Trodelvy head-to-head differentiation gap
DXd manufacturing supply normalization	Moderate (55–65% on schedule)	★★★★ (4)	Operational	CMO capacity additions; regulatory GMP compliance timelines
Enhertu HER2-ultralow label expansion	High (75–80%)	★★★ (3)	Competitive benchmark	DESTINY-Breast06 OS data maturity
Chinese ADC (SKB264/RC48) US approval	Low-Moderate (40–50%)	★★★ (3)	Competitive / pricing	FDA manufacturing inspection; tolerability profile at US doses

So what / Decision implied: The three highest-impact events — I-DXd approval, HER3-DXd NDA, and the Keytruda 1L SCLC combo readout — collectively define 70% of the Merck collaboration's 2026–2028 risk/reward profile. Managing these three events is the job; everything else is noise at this stage of the platform lifecycle.

4. Scenario Analysis: Base, Bull, and Bear Cases

4.1 Base Case — Phased Approvals, Constrained Combo Upside

Probability: ~50%

I-DXd receives accelerated approval in SCLC in October 2026 with a label that includes an ILD monitoring requirement and restricts to patients with ≥ 2 prior lines of therapy. Supply constraints from the May 2026 manufacturing plan changes limit peak 2026 revenues to below consensus estimates, with normalization by mid-2027. HER3-DXd achieves NDA submission in H1 2027 and approval by Q4 2027 in EGFR-mutant NSCLC, capturing a meaningful but niche segment of the post-osimertinib market (estimated 30,000–40,000 annual US patients). The Keytruda combination program in SCLC produces a positive interim signal in H2 2027 but does not achieve the magnitude of OS benefit needed to displace platinum-etoposide plus immune checkpoint combinations as standard of care by 2028. R-DXd CDH6 data are encouraging but not pivotal-ready; ovarian cancer remains a 2028–2029 story. Sac-TMT achieves approval in HR+ breast cancer but faces entrenched Trodelvy preference among community oncologists and does not capture majority TROP2 market share within 24 months of launch. Datroway's NSCLC position stabilizes but does not grow materially versus Keytruda-containing regimens. Chinese ADC entrants remain outside the US market in this window.

4.2 Bull Case — Combo Approvals, Supply Resolution, Platform Re-rating

Probability: ~25%

I-DXd approval arrives on schedule with a label that does not include restrictive ILD boxed warnings beyond existing class language, and manufacturing supply issues resolve faster than the Enhertu precedent (i.e., within 9 months rather than 18) due to proactive CMO capacity additions executed in the May 2026 manufacturing plan. The Keytruda + I-DXd SCLC Phase 3 interim in H2 2027 shows a statistically significant OS improvement over standard of care, triggering a supplemental NDA and potentially the first ADC + PD-1 co-approval with a joint label. HER3-DXd approval in NSCLC arrives Q3 2027 and receives Breakthrough Therapy designation for a second breast cancer indication by year-end 2027,

driving material re-rating of the collaboration's peak sales potential toward \$15–18 billion annually across assets. R-DXd Phase 2 interim data in ovarian cancer demonstrates ORR >35% with manageable safety, positioning for a Phase 3 go-forward decision and attracting additional partnership interest. Enhertu's HER2-ultralow label expansion further entrenches the DXd class as the dominant ADC platform globally, benefiting the Merck assets through halo effects in oncology community credibility. CMS does not select any DXd asset for IRA negotiation prior to 2028, preserving pricing power.

4.3 Bear Case — Regulatory Setback, Supply Disruption, Competitive Erosion

Probability: ~25%

The FDA issues a Complete Response Letter for I-DXd in October 2026, citing insufficient durability of response in the single-arm dataset and requesting randomized confirmation — a scenario consistent with FDA's tightening of accelerated approval standards following the oncology advisory committee guidance revisions of 2024. This single event resets the DXd narrative for the Merck collaboration and triggers a re-evaluation of whether B7-H3 is a validated target at the required expression threshold in SCLC. Separately, the May 2026 manufacturing changes reveal a GMP compliance gap at a key DXd payload production facility, delaying HER3-DXd NDA submission into H2 2027 and creating a 12-month gap where no new DXd approvals occur in the US. Sac-TMT's TROP2 Phase 3 data show non-inferior but not superior efficacy versus Trodelvy, resulting in a label without differentiated positioning and a pricing discount requirement from major PBMs. Kelun-Biotech's MSD-partnered SKB264 achieves US Phase 3 data by Q2 2027 that are competitive with Datroway in NSCLC, introducing a lower-cost TROP2 alternative that compresses the addressable market for both Datroway and Sac-TMT. RemeGen's RC48 receives FDA approval in urothelial cancer with a competitive label, displacing Padcev as a preferred HER2-directed ADC in bladder cancer and establishing Chinese ADC credibility with US oncologists for the first time. IRA drug price negotiation is applied to Enhertu in the 2028 negotiation cycle, creating a payer-level precedent that constrains DXd asset pricing across the portfolio.

The asymmetry across these scenarios is notable: the bull case upside is real but requires three independent positive events to co-occur (combo approval, supply resolution, R-DXd signal), while the bear case requires only one significant failure (I-DXd CRL) to cascade into a multi-asset narrative reset. This asymmetry is characteristic of platform bets, not individual asset bets — it is the fundamental reason the Merck collaboration commanded such a large upfront premium and why the October 2026 PDUFA date carries disproportionate symbolic weight beyond its standalone commercial value.

So what / Decision implied: At current valuations, the bear case is underpriced by the market; the CRL scenario for I-DXd is structurally plausible given FDA's post-2024 accelerated approval scrutiny, and risk-adjusted models that assign it less than 20% probability are optimistic. Hedging through options structures or staged milestone payments in any new collaboration is the implied action for acquirers.

5. Competitive Risks: Tolerability, Differentiation, and Pricing Pressure

5.1 The ILD Problem Is Not Solved — It Is Managed

Interstitial lung disease remains the class-defining safety challenge for DXd-based ADCs. Enhertu's clinical development program established the current standard of ILD monitoring with CT surveillance and grade-based dosing interruptions, and this framework has been carried forward into I-DXd, HER3-DXd, and R-DXd trials. The practical effect is that DXd ADCs carry a management overhead in community oncology settings — where pulmonology consultation access is variable — that newer platforms without ILD risk profiles can use as a differentiating message. Sacituzumab govitecan (Trodelvy) and its next-generation analog sacituzumab tirumotecan compete partly on the absence of significant ILD signal, even if their overall tolerability profiles carry different challenges (hematologic toxicity, diarrhea). For payers constructing utilization management criteria, ILD risk provides a legitimate clinical justification for restricting DXd use to

academic or high-volume community centers, which would structurally limit market penetration relative to open-access SN-38-based ADC regimens.

5.2 Trodelvy and TROP2: The Floor, Not the Ceiling

Sacituzumab govitecan (Trodelvy, Gilead) has established the TROP2 market as real and commercially viable in TNBC and urothelial cancer, but its position in HR+/HER2- breast cancer — where Sac-TMT and Datroway both compete — is less entrenched than in TNBC due to competition from CDK4/6 inhibitors, AKT inhibitors, and PARP inhibitors in the sequencing landscape. The critical differentiation variable for Sac-TMT versus Trodelvy is not efficacy magnitude (both deliver clinically meaningful ORR in the 30–40% range in pre-treated HR+ disease) but tolerability profile and infusion schedule. Sac-TMT's once-every-three-weeks dosing versus Trodelvy's twice-monthly schedule is a genuine commercial advantage in patient and practice preference research, but it is insufficient to command a price premium unless the payer community agrees — and that agreement will depend on head-to-head data that do not currently exist. The FDA's guidance on expedited programs makes clear that PFS or ORR endpoints can support accelerated approval, but OS data will be required for full approval and are the ultimate arbiter of payer willingness to establish preferred formulary position.

5.3 Chinese ADC Entrants: The Structural Repricing Risk

The entry of Kelun-Biotech (SKB264, now partnered with Merck & Co. for ex-China rights) and RemeGen (RC48 disitamab vedotin) into the US competitive landscape represents a qualitatively different threat than previous biosimilar competition. These are not structural copies of approved drugs — they are independently designed ADCs with differentiated linker-payload combinations targeting the same antigens as approved Western agents. SKB264's belzutifan-independent TROP2 mechanism and RC48's HER2 targeting at epitopes distinct from trastuzumab create genuine clinical differentiation arguments, but their most potent competitive weapon is cost. Chinese ADC manufacturing infrastructure, now achieving GMP compliance at scale through NMPA-inspected facilities, enables cost-of-goods structures that Western companies cannot match without fundamental supply chain restructuring. If even one Chinese-origin ADC achieves US approval with an acceptable safety profile in 2026–2027, it will establish a pricing reference point that PBMs will use in every subsequent ADC formulary negotiation, compressing the commercial runway for DXd assets in shared indications by an estimated 15–25% in net price.

Operator Insight — RemeGen RC48 Precedent Watch: RC48's regulatory trajectory in the US is the most important Chinese ADC data point of 2026–2027. If it achieves approval in urothelial cancer, the institutional credibility established with US oncologists will accelerate market acceptance for subsequent Chinese ADC entrants in a way that no amount of Western competitive messaging can prevent. BD teams assessing TROP2 or HER2 ADC acquisitions must stress-test against a world where a Chinese-origin agent is on formulary at 30–40% below DXd list pricing within 24 months of the deal close.

5.4 Competitive Heatmap: DXd vs. Field

Dimension	DXd Platform (Merck/DSC)	Enhertu/Datroway (AZ/DSC)	Trodelvy / Sac-TMT (Gilead/Kelun)	Chinese ADCs (RC48, SKB264)
Efficacy Depth	High — deep ORR, durable responses in HER2/HER3/B7-H3	Best-in-class — OS data in HER2; standard-setting	Moderate-High — strong ORR in TNBC; OS data maturing	Moderate — early US data; comparable ORR claimed
Tolerability Profile	ILD risk (class); manageable with protocol; limits community use	ILD risk (established management); label well-characterized	Hematologic / GI toxicity; no significant ILD; community-friendly	Variable; RC48 neuropathy signal; SKB264 ILD signal emerging

Combo Potential with I-O	High potential (Keytruda strategy); unproven in pivotal data	DESTINY-Breast09 exploring; signals positive	Limited synergy data; some TROP2 + PD-L1 signals	Early combination studies; no pivotal data
Manufacturing / Supply	At risk — May 2026 plan changes; DXd payload complexity	Stabilized — AZ CMO network mature after 2021 normalization	More established — SN-38 payload infrastructure mature	GMP compliance risk in US inspections; lower COGS if approved
Pricing Power / Payer Position	Strong near-term; IRA risk 2028+; combo economics unclear	Strong; IRA negotiation risk accelerating for Enhertu	Moderate; Trodelvy losing share in some indications	Structural discount likely; defines market floor pricing
Breadth of Pipeline	4+ indications in development; B7-H3 novel target	3+ indications; HER2-ultralow expansion ongoing	2–3 indications; TROP2 market definition largely complete	Narrow — 1–2 indications in US development

So what / Decision implied: DXd's competitive moat is real but narrowing on tolerability and pricing dimensions faster than platform advocates acknowledge. The combination strategy with Keytruda is the primary mechanism to create an insurmountable differentiation gap — absent that data, the field converges toward commodity competition on TROP2 and HER3 by 2028–2029.

6. Operator Precedents: ADC Launch Patterns and Failure Modes

The history of ADC development contains enough failures to generate a reliable failure-mode taxonomy, and the DXd platform's risk profile maps onto several of them with uncomfortable precision. The most instructive precedents span three categories: supply-constrained launches, tolerability-driven label restrictions, and indication-specific clinical failures despite mechanistic promise.

Enhertu's 2019–2021 supply constraints have been cited above, but the mechanism is worth specifying for operators: the DXd payload requires multi-step enzymatic conjugation under controlled conditions that creates a manufacturing yield curve distinct from conventional small-molecule drug substance production. Early in any new ADC program, conjugation process consistency is the rate-limiting step, not antibody production capacity. The May 2026 manufacturing plan changes for the Merck collaboration assets suggest that this yield consistency issue has recurred at a different point in the platform's expansion — specifically, scaling from Phase 3 trial quantities to commercial supply volumes across three assets simultaneously, which no ADC manufacturer has successfully executed without at least one supply disruption event.

The most cautionary failure precedent for I-DXd specifically is not another B7-H3 program — it is rovalpituzumab tesirine (Rova-T), AbbVie's DLL3-targeted ADC in SCLC, which failed Phase 3 in 2018 after promising Phase 1 signals. Rova-T's failure was attributed to a combination of target expression heterogeneity in SCLC tumors, a subtherapeutic dosing window created by off-target toxicity, and a clinical trial design that did not adequately select for DLL3-high patients. I-DXd's B7-H3 program has learned from this failure — B7-H3 is more uniformly expressed than DLL3, and patient selection has been refined — but the SCLC microenvironment's resistance mechanisms are not fully characterized, and the single-arm trial supporting the October 2026 PDUFA does not have the randomized comparator data that would definitively establish whether observed responses are target-dependent or driven by the DXd payload mechanism in a highly treatment-sensitive tumor biology.

Conversely, the positive precedent for accelerated approval in heavily pre-treated solid tumors with single-arm data is established through the FDA's approval of Enhertu in HER2-low breast cancer and multiple prior ADC approvals where

ORR and DoR were deemed sufficient to establish clinical benefit in the absence of a randomized comparator. The FDA's expedited programs framework — Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review — has been consistently applied to ADC programs that demonstrate ORR in populations with no remaining standard-of-care options, and I-DXd's SCLC target population at third-line and beyond squarely meets this criterion. The regulatory risk is not that the FDA will decline to use Accelerated Approval; it is that the FDA will require a more restrictive label than expected (limiting to DLL3-high-analogous B7-H3-high patients, for example) or will demand earlier confirmatory data submission timelines that constrain the commercial window.

Operator Insight — Mylotarg Redux Risk: Gemtuzumab ozogamicin (Mylotarg) was voluntarily withdrawn in 2010 after a Phase 3 trial failed to confirm clinical benefit and showed increased mortality versus control — then re-approved in 2017 with a lower dose and improved patient selection. The lesson for DXd operators is that accelerated approvals in oncology are genuine regulatory risk events, not rubber stamps, and the confirmatory trial design is more important than the approval itself for long-term commercial viability. The IDEate-Lung03 design for I-DXd + Keytruda in 1L SCLC is the confirmatory anchor — if it is not powered to show OS benefit over the existing atezolizumab/durvalumab + chemotherapy standard, the accelerated approval has a structural fragility that competitors and payers will exploit.

So what / Decision implied: Commercial teams launching I-DXd in Q4 2026 should build their market access strategy around the confirmatory trial readout timeline, not the accelerated approval label alone. Any account that requires OS evidence before prescribing (major academic centers, IDN formulary committees) will not be accessible until 2027–2028 regardless of October 2026 approval.

7. Strategic Implications for BD/M&A

The Merck/Daiichi Sankyo collaboration's structure has effectively taken the DXd platform itself off the M&A market for the assets under agreement. What remains available — and what should be of primary BD interest — is the layer of ADC innovation that the DXd platform has not addressed: novel targets beyond B7-H3, HER3, and CDH6; next-generation payloads beyond DXd that avoid the ILD liability; and bispecific ADC constructs that can address tumor heterogeneity without requiring high uniform target expression. These represent the white spaces where acquirers can still build differentiated positions without competing directly against a \$22 billion platform.

The BD calculus for Chinese ADC assets has become particularly complex. Merck's own licensing of SKB264 from Kelun-Biotech for ex-China rights establishes that US large-cap pharma is willing to license Chinese-origin ADCs, normalizing the practice and removing the reputational barrier that previously deterred similar deals. The implication for other potential acquirers is that the window for securing ex-China rights to the most commercially attractive Chinese ADC programs is narrowing rapidly — assets that were available at reasonable valuations in 2024 are now receiving competitive term sheets from multiple Western counterparties. Acquirers who missed the Kelun window should be evaluating RemeGen, Mabworks, and Innovent's ADC programs on accelerated timelines.

The supply chain dimension of any ADC M&A transaction deserves more emphasis than it typically receives in term sheets. An acquired ADC asset's CMC (chemistry, manufacturing, and controls) package is as value-determinative as its clinical data, because the FDA's GMP requirements for ADC manufacturing — particularly for DXd-class payloads with potent cytotoxic warheads — create a regulatory pathway where manufacturing deficiencies can delay approval by 12–24 months independently of clinical data quality. Any BD team that does not conduct a CMC-specific due diligence parallel to clinical diligence is structurally underinformed about asset value.

The IRA drug price negotiation mechanism introduces a new BD variable that did not exist in prior ADC deal cycles. Assets approved before 2026 in indications with large Medicare populations are now exposed to negotiation timelines that cap pricing power 7–9 years post-approval for small molecules and 11–13 years for biologics. Enhertu's HER2 breast cancer indication, with its large Medicare-eligible patient population, is approaching the negotiation exposure window. Any acquirer modeling DXd-class ADC peak sales beyond 2030 must build in a price negotiation haircut for indications

with >50% Medicare coverage — a factor that reduces peak net revenue assumptions by an estimated 20–35% in large breast cancer and NSCLC indications under current IRA mechanics.

So what / Decision implied: The most attractive BD targets in the ADC space today are not the DXd follow-on programs — they are: (1) novel payload platforms that solve the ILD problem while maintaining efficacy, (2) ex-China rights to second-tier Chinese ADC programs before competitive term sheet pressure peaks in 2026, and (3) bispecific ADC constructs in small or mid-size indications with orphan or rare disease designations that provide pricing protection against IRA negotiation mechanics.

8. Investment Thesis with Reversibility Scoring

An investment thesis in the ADC space in 2026 must account for four distinct risk layers simultaneously: clinical (does the drug work?), regulatory (will FDA approve it on the expected timeline and label?), commercial (will payers reimburse it without restrictions that limit addressable volume?), and operational (can the drug be manufactured and distributed at scale without supply constraints that delay revenue normalization?). The DXd platform scores well on the first two dimensions and poorly on the fourth; the Trodelvy/Sac-TMT competitive cluster scores better on the fourth but worse on the second in large indications. Chinese ADC entrants score lowest on the second and third dimensions but have structural long-term cost advantages on the fourth that Western platforms cannot replicate without supply chain transformation.

Asset / Thesis	Clinical Conviction	Regulatory Confidence	Commercial Confidence	Operational Confidence	Reversibility Score (1=irreversible, 5=easily reversed)	Net Thesis
I-DXd SCLC accelerated approval	High	Moderate-High (Oct 2026 PDUFA)	Moderate (supply-gated)	Low (May 2026 mfg risk)	2 — CRL is hard to reverse within 12 months	Conditional Buy — only if supply plan is credible
HER3-DXd NSCLC post-osimertinib	High (mechanistically sound)	Moderate-High (NDA 2027)	High (EGFR-mut population well-defined)	Moderate (DXd platform mfg risk inherited)	3 — approval delay painful but recoverable	Strong Hold/Add — best risk/reward in portfolio
R-DXd CDH6 ovarian	Speculative (CDH6 biology unproven)	Low-Moderate (2028+)	High if data work (high unmet need)	Low-Moderate	4 — Phase 2 failure containable; not a platform-killer	Option Value Only — do not capitalize at full DCF
Sac-TMT TROP2 breast	Moderate-High	Moderate (crowded field risk)	Moderate (Trodelvy entrenchment)	High (SN-38 infrastructure mature)	4 — can reposition to 2L/3L if 1L fails	Hold — differentiation thesis needs head-to-head data
Chinese ADC (ex-China licensing)	Moderate	Low-Moderate (US GMP risk)	High if approved (price disruption)	High (low COGS)		

